

### REMARKS

The Examiner rejected claims 1-34. Claim 31 has been cancelled herein, and claims 25 and 33 have been amended. Thus, claims 1-30 and 32-34 are pending. The application as originally filed supports these amendments. For example, page 2, lines 28-30 disclose grape skin extract:grape seed extract ratios. Thus, no new matter has been added. In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1-30 and 32-34.

#### Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 1-34 under 35 U.S.C. § 102(b) as being unpatentable over Perkes (WO 99/07400). Specifically, the Examiner stated that Perkes disclosed:

a dietary supplement comprising an enzyme that is effective for inhibiting in vivo platelet activity and LDL cholesterol oxidation in a mammal at a dosage of about 30 mg/kg or less. The supplement may contain grape seed extracts, grape skin extracts, bilberry extracts, ginkgo biloba extracts or quercetin. The supplement may also contain fungal proteases, acid stable proteases and bromelain (Abstract). Perkes teaches every aspect of applicant's claimed invention. Thus Perkes anticipates claims 1-34.

Applicants respectfully disagree. A claim is anticipated under § 102(b) only if each and every limitation is disclosed in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 639 (Fed. Cir. 1989) and MPEP § 2131. Claims 1-24 are directed to a dietary supplement comprising a grape skin extract and a Muscat variety grape seed extract. The Perkes reference does not disclose such a supplement. In fact, at no point does the Perkes reference disclose a supplement containing a Muscat grape seed extract. Thus, the Perkes reference does not anticipate claims 1-24.

Claims 25-30, as amended, recite a dietary supplement comprising a grape skin extract and a grape seed extract where the ratio of the grape skin extract to the grape seed extract is between 3 to 1 and 5 to 1. None of the compositions disclosed in the Perkes reference has such a ratio. In fact, the three specific formulations disclosed in the Perkes reference have ratios (1.66 to 1, see page 17; 1.2 to 1, see page 19; and 20.5 to 1, see page 21) well outside the range of

ratios presently recited in the claims. Thus, the Perkes reference does not anticipate claims 25-30.

Claim 32 is directed to a dietary supplement comprising a grape skin extract and a grape seed extract where the grape seed extract comprises (1) at least about 3.5 percent monomeric flavanols, (2) at least about 60 percent oligomeric flavanols, and (3) less than about 35 percent polymeric flavanols. At no point does the Perkes reference disclose making such a supplement. Thus, the Perkes reference does not anticipate claim 32.

Claims 33-34, as amended, are directed to a method of inhibiting platelet aggregation or LDL cholesterol oxidation in a mammal. The method requires administering either (1) a dietary supplement containing a grape skin extract and a Muscat variety grape seed extract, (2) a dietary supplement containing a grape skin extract and a grape seed extract where the ratio of grape skin extract to grape seed extract is between 3 to 1 and 5 to 1, or (3) a dietary supplement containing a grape skin extract and a grape seed extract where the grape seed extract contains at least about 3.5 percent monomeric flavanols, at least about 60 percent oligomeric flavanols, and less than about 35 percent polymeric flavanols. At no point does the Perkes reference disclose such dietary supplements, let alone the administration of such supplements to inhibit platelet aggregation or LDL cholesterol oxidation in a mammal. Thus, the Perkes reference does not anticipate claims 33-34.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1-30 and 32-34 under 35 U.S.C. § 102(b).

#### Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-34 under 35 U.S.C. § 103(a) as being unpatentable over Perkes (WO 99/07400). Specifically, the Examiner stated:

The disclosed invention provides a dietary supplement comprising an enzyme that is effective for inhibiting in vivo platelet activity and LDL cholesterol oxidation in a mammal at a dosage of about 30 mg/kg or less. The supplement may contain grape seed extracts, grape skin extracts, bilberry extracts, ginkgo biloba extracts or quercetin. The supplement may also contain fungal proteases, acid stable proteases and bromelain (Abstract).

Applicants respectfully disagree. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, and (2) whether the prior art would also have revealed that in so making, those of ordinary skill would have had a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Claims 1-24 are directed to a dietary supplement comprising a grape skin extract and a Muscat variety grape seed extract. The Perkes reference discloses three formulations containing grape skin extracts and grape seed extracts. The Perkes reference, however, does not teach or suggest any composition containing a grape skin extract in combination with a Muscat variety grape seed extract, as present claims 1-24 require. Thus, the cited reference fails to suggest to those having ordinary skill in the art that they should make the presently claimed invention. Thus, claims 1-24 are not obvious.

*Ratio*  
Claims 25-30, as amended, recite a dietary supplement comprising a grape skin extract and a grape seed extract where the ratio of the grape skin extract to the grape seed extract is between 3 to 1 and 5 to 1. At no point does the Perkes reference teach or suggest making a supplement having such a ratio of grape skin extract to grape seed extract. In fact, a person having ordinary skill in the art reading the Perkes reference would not have been motivated to make a supplement having a grape skin extract to grape seed extract ratio between 3 to 1 and 5 to 1. This is especially true given that the three specific formulations exemplified in the Perkes reference have ratios (1.66 to 1, see page 17; 1.2 to 1, see page 19; and 20.5 to 1, see page 21) well outside the range of ratios presently recited in the claims. Thus, claims 25-30 are not obvious.

Claim 32 is directed to a dietary supplement containing a grape skin extract and a grape seed extract where the grape seed extract contains (1) at least about 3.5 percent monomeric flavanols, (2) at least about 60 percent oligomeric flavanols, and (3) less than about 35 percent polymeric flavanols. The Perkes reference discloses grape seed and grape skin extracts, bilberry extracts, ginkgo biloba extracts, or quercetin as flavonoid sources for use in dietary supplements. The Perkes reference, however, does not teach or suggest a grape seed extract having (1) at least about 3.5 percent monomeric flavanols, (2) at least about 60 percent oligomeric flavanols, and (3) less than about 35 percent polymeric flavanols. Nowhere in the Perkes reference are the

relative amounts of the flavanols in any grape seed extract mentioned, and nowhere in the Perkes reference is it suggested to make or use particular types of flavanols, never mind in the grape seed extract itself. Instead, the Perkes reference discloses a grape seed extract as one possible flavanol source among others, including bilberry, ginkgo biloba, and quercetin. In fact, the Perkes reference provides no teaching or suggestion of the desirable relative percentages of monomeric, oligomeric, and polymeric flavanols in a grape seed extract, as its flavanols may be derived from multiple independent sources. Thus, a person having ordinary skill in the art reading the Perkes reference would not have been motivated to make or use the presently claimed supplements.

Claims 33-34, as amended, are directed to a method of inhibiting platelet aggregation or LDL cholesterol oxidation in a mammal. The method requires administering either (1) a dietary supplement containing a grape skin extract and a Muscat variety grape seed extract, (2) a dietary supplement containing a grape skin extract and a grape seed extract where the ratio of grape skin extract to grape seed extract is between 3 to 1 and 5 to 1, or (3) a dietary supplement containing a grape skin extract and a grape seed extract where the grape seed extract contains at least about 3.5 percent monomeric flavanols, at least about 60 percent oligomeric flavanols, and less than about 35 percent polymeric flavanols. As discussed above, the Perkes reference fails to suggest that a person having ordinary skill in the art should make the presently claimed dietary supplements. Moreover, at no point does the Perkes reference teach or suggest administering such supplements to inhibit platelet aggregation or LDL cholesterol oxidation in a mammal. Thus, claims 33-34 are not obvious.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1-30 and 32-34 under 35 U.S.C. § 103(a).

The Examiner also rejected claims 1-13, 16-19, and 21-32 under 35 U.S.C. § 103(a) as being unpatentable over Gaynor *et al.* (U.S. Patent No. 5,904,924). Specifically, the Examiner stated that Gaynor discloses a nutritional powder comprised of a grape seed extract and a grape skin extract, with the grape seed extract standardized to 95% polyphenols. The Examiner also stated that the formulation of Gaynor *et al.* includes Japanese Green tea (standardized to 7.5% epigallocatechin gallate), bilberry (standardized to 25% anthocyanocides), and Ginkgo Biloba

(standardized to 24% ginkgo flavoglycosides). After acknowledging that the reference does not expressly teach Applicant's claimed "ratio," the Examiner stated that "differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical." In addition, the Examiner concluded that one of ordinary skill in the art at the time of the invention would have been motivated to modify the teachings of Gaynor with the "expectation that the components of the referenced composition have been conventionally employed for their known functions or nutritional benefit, such as antioxidant and anti-tumor activity."

Applicants respectfully disagree. Claims 1-13, 16-19, and 21-24 are directed to a dietary supplement containing a grape skin extract and a Muscat variety grape seed extract. The Gaynor *et al.* reference discloses a 969 gram mixture of 55 dried ingredients ranging from bee pollen and dandelion to biotin and inositol. The reference also lists one of the 55 ingredients as being a "grape skin extract," and another as being a "grape seed extract." The reference, however, does not teach or suggest a supplement having a Muscat variety grape seed extract, as present claims 1-13, 16-19, and 21-24 require. In fact, at no point does the cited reference mention the use of a Muscat variety grape seed extract. Thus, the cited reference does not render claims 1-13, 16-19, and 21-24 obvious.

Claims 25-30, as amended, recite a dietary supplement containing a grape skin extract and a grape seed extract where the ratio of grape skin extract to grape seed extract is between 3 to 1 and 5 to 1. At no point does the Gaynor *et al.* reference disclose any such composition. In fact, the only composition disclosed in the Gaynor *et al.* reference is the 969 gram mixture containing 300 mg of grape skin extract and 40 mg of grape seed extract, which represents a 7.5 to 1 ratio of grape skin extract to grape seed extract. The Gaynor *et al.* reference fails to teach or suggest any other ratio of grape skin extract to grape seed extract. Moreover, at no point does the Gaynor *et al.* reference teach or suggest that a person having ordinary skill in the art should modify the amounts of grape skin extract and grape seed extract disclosed in the Gaynor *et al.* reference to obtain a supplement as presently claimed. Thus, claims 25-30 are not obvious.

After acknowledging that the Gaynor *et al.* reference fails to disclose the claimed ratios, the Examiner asserted that the discovery of the optimum or workable ranges by routine experimentation is not inventive absent a showing of criticality. Applicants respectfully disagree

with the Examiner's assertion, but nevertheless note that the Applicants' specification sets forth the surprising synergistic effects discovered with respect to the presently claimed ratios. In particular, Examples 2 and 3 at pages 14-15 demonstrate that the inhibition of platelet aggregation by grape skin extracts alone is about 3- to 5-fold weaker than that by grape seed extracts alone. Example 4, entitled "Synergy between grape seed extract and grape skin extract," at pages 17-18, demonstrates synergistic (70%) platelet aggregation inhibition at a 5:1 ratio of grape skin extract:grape seed extract, with only minimal inhibition (10%) for the grape seed extract alone, and virtually no inhibition for the grape skin extract alone. Thus, Applicants demonstrated a surprising synergy of interaction between grape skin extracts and grape seed extracts in platelet aggregation inhibition.

Claim 32 is directed to a dietary supplement containing a grape skin extract and a grape seed extract where the grape seed extract contains (1) at least about 3.5 percent monomeric flavanols, (2) at least about 60 percent oligomeric flavanols, and (3) less than about 35 percent polymeric flavanols. The Gaynor *et al.* reference does not teach or suggest a grape seed extract containing the recited amounts of particular flavanols. Instead, the Gaynor *et al.* reference discloses grape seed extract as one component of 55 in its formulation, and notes only that the grape seed extract is standardized to 95% polyphenols. Nowhere in the Gaynor *et al.* reference are the relative amounts of the flavanols in any grape seed extract mentioned, and nowhere in the Gaynor *et al.* reference is it suggested to make or use particular types of flavanols, never mind in the grape seed extract itself. Thus, a person having ordinary skill in the art reading the Gaynor *et al.* reference would not have been motivated to make or use the presently claimed supplements.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1-13, 16-19, 21-30, and 32 under 35 U.S.C. § 103(a).

### CONCLUSION

Applicants submit that claims 1-30 and 32-34 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. Filed herewith is a check in payment of the Petition for Automatic Extension with the required fee. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.


Applicant : Suk Cho et al.  
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Attached is a marked-up version of the changes being made by the current amendment.

Respectfully submitted,

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**Version with markings to show changes made**

**In the claims:**

Claim 31 has been cancelled.

Claims 25 and 33 have been amended as follows:

25. (Amended Once) A dietary supplement comprising a grape skin extract and a grape seed extract, wherein the ratio of said grape skin extract to said grape seed extract is between 3 to 1 and 5 [10] to 1.

33. (Amended Once) A method of inhibiting platelet aggregation or LDL cholesterol oxidation in a mammal, said method comprising administering a dietary supplement to said mammal, wherein said dietary supplement is selected from the group consisting of:

(a) a dietary supplement comprising a grape skin extract and a Muscat variety grape seed extract,

(b) a dietary supplement comprising a grape skin extract and a grape seed extract, wherein the ratio of said grape skin extract to said grape seed extract is between 3 to 1 and 5 [10] to 1,

“(c) a dietary supplement comprising a grape skin extract and a grape seed extract, wherein said grape seed extract comprises at least about 70 percent polyphenolics,] and

(c)[(d)] a dietary supplement comprising a grape skin extract and a grape seed extract, wherein said grape seed extract comprises at least about 3.5 percent monomeric flavanols, at least about 60 percent oligomeric flavanols, and less than about 35 percent polymeric flavanols.